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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/626,275	07/24/2003	Ernest J. Lee	PC28017	9606

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EXAMINER	
SCHLIENTZ, NATHAN W	
ART UNIT	PAPER NUMBER
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/626,275	LEE ET AL.	
	Examiner	Art Unit	
	Nathan W. Schlientz	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-27* is/are pending in the application.

4a) Of the above claim(s) *26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Claims

Claim 2 has been cancelled in an amendment filed 26 November 2008. As a result, claims 1 and 3-25 are examined herein on the merits for patentability. Claims 26-27 remain withdrawn from further consideration as being directed to non-elected subject matter. No claim is allowed at this time.

Withdrawn Rejections

Rejections and/or objections not reiterated from the previous Office Action are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 3-7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, claims 3-7 are dependent from claim 2, which is a cancelled claim. Therefore, the metes and bounds of claims 3-7 are not

clearly defined. The examiner is construing claims 3-7 as being dependent from claim 1 since the limitations of claim 2 were incorporated into claim 1.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Claims 1-16 and 18-25 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Claims 1-23 of copending Application No. 10/626,166. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to a pharmaceutical composition comprising pramipexole and a pharmaceutically acceptable excipient. Accordingly, the scope of the copending claims overlap and thus they are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

An attorney or agent, not of record, is not authorized to sign a terminal disclaimer in the capacity as an attorney or agent acting in a representative capacity as provided by 37 CFR 1.34 (a). See 37 CFR 1.321(b) and/or (c).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in Graham v. John Deere Co., 383 U.S. 1,148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1 and 3-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pospisilik '240 (US 2002/0103240) in view of Ju (US 6,197,339) (cited in the IDS filed 22 September 2003).

Applicant claims:

Applicants claim an orally deliverable composition comprising pramipexole and at least one pharmaceutically exceptable excipient wherein the composition exhibits an *in vitro* release profile such that at 2 hours no more than about 20% has dissolved, or an *in vivo* absorption profile such that the time to reach a mean of 20% absorption is greater than 2 hours and/or the time to reach 40% absorption is greater than 4 hours. Applicants also claim the composition above in the form of discrete dosage units sufficient to provide a daily dosage in one to a small plurality of dosage units administered at one time.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Pospisilik '240 teaches controlled release pellet or tablet compositions may be produced using pramipexole comprising a mixture of pramipexole salt, a suitable filler, such as microcrystalline cellulose, and a suitable release controlling agent comprising water and/or a water-insoluble macromolecular substance such as an acrylate polymer or a modified cellulose ([0064]). Pospisilik '240 further teaches that pramipexole is commercially available as the dihydrochloride salt ([0004]).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Pospisilik '240 does not teach the controlled release pramipexole to have an *in vitro* release profile wherein at 2 hours no more than 20% pramipexole has dissolved, or an *in vivo* absorption profile wherein the time to reach a mean of 20% absorption is

greater than about 2 hours and/or the time to reach a mean of 40% absorption is greater than about 4 hours, as instantly claimed.

However, Ju teaches a sustained release formulation comprising 0.3-16% R)-5,6-dihydro-5-(methylamino)-4H-imidazo[4,5-ij]-quinolin-2(1H)-one (Z)-2-butenedioate (1:1) (sumanirole maleate), 60-69% starch and 30-40% hydroxypropylmethylcellulose, wherein the starch is preferably pregelatinized starch and the HPMC is preferably HPMC 2208 USP 4,000 cps or HPMC 2910 USP 4,000 cps (col. 2, ll. 1-60).

Pramipexole and sumanirole maleate are both dopamine D_2 receptor agonists useful in the treatment of Parkinson's disease (instant specification pages 1 and 2, paragraphs [0003] and [0007]; and Ju col. 1, ll. 14-24).

Pospisilik '240 also does not teach the controlled release pramipexole wherein the pramipexole is in the form of a dosage unit that is given as a daily dose in one to a small plurality of dosage units administered at one time, as instantly claimed.

However, Ju teaches that the exact dosage and frequency of administration depends on the severity of the condition being treated, the weight, general physical condition of the particular patient, and other medication the individual may be taking, as is well-known to those skilled in the art and can be more accurately determined by measuring the blood level or concentration of the drug in the patient's blood and/or the patient's response to the particular condition being treated (col. 3, ll. 45-54).

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to formulate the controlled release pellet or tablet compositions comprising pramipexole dihydrochloride salt, as taught by Pospisilik '240, further comprising 60-69% starch and 30-40% hydroxypropylmethylcellulose, as reasonably taught by Ju. It would also have been *prima facie* obvious for one of ordinary skill in the art to determine the appropriate dosage unit and administration frequency, as reasonably taught by Ju.

It is noted that Ju does not teach the *in vitro* release profile and *in vivo* absorption profile that result from starch and HPMC sustained release formulations. However, the formulations comprise the same starch and HPMC compounds in the same amounts as the compounds of the instant application (instant specification pages 10-11, paragraphs [0052]-[0059]). Therefore, the sustained release formulations would inherently possess the *in vitro* release profile and *in vivo* absorption profile as instantly claimed.

The examiner respectfully points out the following from MPEP 2112: "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court stated that "just as the discovery of properties of a known material does

not make it novel, the identification and characterization of a prior art material also does not make it novel."

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicants argue on page 6 that Pospisilik '240 contains no disclosure of the claimed *in vitro / in vivo* release profiles of the present invention, and contains no suggestion that its alleged controlled-release formulations are suitable for once-daily administration. Applicants then argue that Ju fails to teach or suggest a once-daily dosage form of pramipexole. However, the examiner respectfully argues that Pospisilik '240 clearly teach that controlled release compositions comprising pramipexole can be formulated with a mixture of a pramipexole salt, a suitable filler, such as microcrystalline cellulose, and a suitable release controlling agent comprising water and/or a water-insoluble macromolecular substance such as an acrylate polymer or a modified cellulose. Therefore, Pospisilik '240 clearly provide motivation for formulating a controlled-release dosage form of pramipexole. Ju teaches that hydroxypropyl methylcellulose has been used extensively for producing sustained release tablet formulations. Ju further teaches that mechanically damaged starch provides delayed, controlled and targeted release formulations. Therefore, it would have been obvious to

use HPMC and modified starch in the controlled release formulations with pramipexole. Also, Ju teaches that the exact dosage and frequency of administration depends on the severity of the condition being treated, the weight, general physical condition of the patient, other medication the patient is taking, as is well known to those skilled in the art and can be more accurately determined by measuring the blood level or concentration of the free base in the patient's blood and/or the patient's response to the particular condition being tested. Therefore, it would be well within the skill of one of ordinary skill in the art to determine the most accurate dosing frequency of a pramipexole controlled release formulation, as reasonably taught by Ju.

Applicants argue that the design of controlled release dosage forms of each individual drug must be individualized to their particular physical and chemical properties. Applicants argue that what may be an effective type of dosage form design for one drug simply is ineffective in promoting the sustained release of another drug. However, the examiner respectfully argues that Pospisilik '240 clearly provides motivation for formulating controlled release drug compositions comprising microcrystalline cellulose and an acrylate polymer or a modified cellulose. Ju teaches that HPMC and pregelatinized starch have been used in the art to formulate controlled release drug compositions. Therefore, one of ordinary skill in the art would have had a reasonable expectation that formulating a pramipexole formulation comprising HPMC and pregelatinized starch would have effectively made a controlled release dosage form having the instantly claimed properties.

It is noted by the examiner that the instant claims are drawn to a composition exhibiting at least one of (a) an *in vitro* release profile wherein on average no more than about 20% of the pramipexole is dissolved within 2 hours, and (b) an *in vivo* pramipexole absorption profile following single dose oral administration to healthy adult humans wherein the time to reach a mean of 20% absorption is greater than about 2 hours and/or the time to reach a mean of 40% absorption is greater than about 4 hours. The claims drawn to a method of administering a sustained release pramipexole formulation once daily have been withdrawn.

2. Claims 1, 3-18 and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pospisilik '119 (US 2004/0068119) in view of Ju (US 6,197,339).

Applicant claims:

Applicants claim an orally deliverable composition comprising pramipexole and at least one pharmaceutically exceptable excipient wherein the composition exhibits an *in vitro* release profile such that at 2 hours no more than about 20% has dissolved, or an *in vivo* absorption profile such that the time to reach a mean of 20% absorption is greater than 2 hours and/or the time to reach 40% absorption is greater than 4 hours. Applicants also claim the composition above in the form of discrete dosage units sufficient to provide a daily dosage in one to a small plurality of dosage units administered at one time.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Pospisilik '119 teaches controlled release pellet or tablet compositions may be produced using pramipexole comprising a mixture of pramipexole salt, a suitable filler, such as microcrystalline cellulose, and a suitable release controlling agent comprising water and/or a water-insoluble macromolecular substance such as an acrylate polymer or a modified cellulose ([0061]). Pospisilik '119 further teaches that pramipexole is commercially available as the dihydrochloride salt ([0004]).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

Pospisilik '119 does not teach the controlled release pramipexole to have an *in vitro* release profile wherein at 2 hours no more than 20% pramipexole has dissolved, or an *in vivo* absorption profile wherein the time to reach a mean of 20% absorption is greater than about 2 hours and/or the time to reach a mean of 40% absorption is greater than about 4 hours, as instantly claimed.

However, Ju teaches a sustained release formulation comprising 0.3-16% R)-5,6-dihydro-5-(methylamino)-4H-imidazo[4,5-ij]-quinolin-2(1H)-one (Z)-2-butenedioate (1:1) (sumanirole maleate), 60-69% starch and 30-40% hydroxypropylmethylcellulose, wherein the starch is preferably pregelatinized starch and the HPMC is preferably HPMC 2208 USP 4,000 cps or HPMC 2910 USP 4,000 cps (col. 2, ll. 1-60).

Pramipexole and sumanirole maleate are both dopamine D_2 receptor agonists useful in the treatment of Parkinson's disease (instant specification pages 1 and 2, paragraphs [0003] and [0007]; and Ju col. 1, ll. 14-24).

Pospisilik '119 also does not teach the controlled release pramipexole wherein the pramipexole is in the form of a dosage unit that is given as a daily dose in one to a small plurality of dosage units administered at one time, as instantly claimed.

However, Ju teaches that the exact dosage and frequency of administration depends on the severity of the condition being treated, the weight, general physical condition of the particular patient, and other medication the individual may be taking, as is well-known to those skilled in the art and can be more accurately determined by measuring the blood level or concentration of the drug in the patient's blood and/or the patient's response to the particular condition being treated (col. 3, ll. 45-54).

Finding of *prima facie* obviousness

Rational and Motivation (MPEP 2142-43)

Therefore, it would have been *prima facie* obvious for one skilled in the art at the time of the invention to formulate the controlled release pellet or tablet compositions comprising pramipexole dihydrochloride salt, as taught by Pospisilik '119, further comprising 60-69% starch and 30-40% hydroxypropylmethylcellulose, as reasonably taught by Ju. It would also have been *prima facie* obvious for one of ordinary skill in the art to determine the appropriate dosage unit and administration frequency, as reasonably taught by Ju.

It is noted that Ju does not teach the *in vitro* release profile and *in vivo* absorption profile that result from starch and HPMC sustained release formulations. However, the formulations comprise the same starch and HPMC compounds in the same amounts as the compounds of the instant application (instant specification pages 10-11, paragraphs

[0052]-[0059]). Therefore, the sustained release formulations would inherently possess the *in vitro* release profile and *in vivo* absorption profile as instantly claimed.

The examiner respectfully points out the following from MPEP 2112: "The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer." *Atlas Powder Co. v. Ireco Inc.*, 190 F.3d 1342, 1347, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999). Thus the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977). In *In re Crish*, 393 F.3d 1253, 1258, 73 USPQ2d 1364, 1368 (Fed. Cir. 2004), the court stated that "just as the discovery of properties of a known material does not make it novel, the identification and characterization of a prior art material also does not make it novel."

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

Applicant's arguments with respect to Pospisilik '119 in view of Ju are the same as above. Therefore, the examiners response above is incorporated herein by reference.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan W. Schlientz whose telephone number is (571)272-9924. The examiner can normally be reached on 9:00 AM to 5:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NWS

/John Pak/
Primary Examiner, Art Unit 1616